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WHAT'S NEW IN INTENSIVE CARE

Delirium versus encephalopathy: a call for precise terminology

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Terminology: delirium versus encephalopathy

Research and clinical care are hampered by the use of numerous terms to describe global cognitive dysfunction due to critical illness [1]. These include delirium, (acute) encephalopathy, acute confusional state, acute brain dysfunction, acute brain failure, and altered mental status. Although there is no evidence that these different terms represent distinct clinical entities, literature on the most frequently used terms, delirium and encephalopathy is highly segregated (Fig. 1, left side) [2]. Delirium-titled articles rarely cite articles with encephalopathy as a title word and seldom mention encephalopathy in the text [2]. These articles are published preferentially in journals of geriatrics, gerontology, psychiatry, psychology, intensive care medicine, or anaesthesiology [2]. Similarly, encephalopathy-titled articles rarely cite papers with delirium as a title word, and rarely mention delirium in the text. These papers are published mainly in journals of neurology, neurosciences, general or internal medicine, or other fields, such as genetics [2].

To overcome problems due to segregation of the literature, a multidisciplinary international expert panel was formed to generate consensus recommendations using the modified Delphi method, which has been endorsed by ten major professional societies. The panel regarded acute encephalopathy to be the pathobiological process in the brain, and coma and delirium as possible phenotypic manifestations of this process (Fig. 1, right side) [2]. It did not recommend the ongoing use of the terms acute confusional state, acute brain dysfunction, acute brain failure, or altered mental status, as they lack precision and additive value [2].

Although these efforts were applauded, others criticized the lack of a term to identify a non-comatose patient who has altered level of alertness not attributable to sedation, in whom delirium cannot reliably be assessed because of the depressed alertness. Delirium, per DSM-5-TR, can only be diagnosed in patients who are sufficiently conscious to assess attention and awareness; thus, coma—defined as unarousable unresponsiveness—excludes a diagnosis of delirium until the patient regains consciousness. It is confusing to use different terms for the underlying substrate (encephalopathy) versus the clinical manifestations thereof (delirium). Oldham and Halloway discussed a theoretical model to highlight a clinical phenotype-related definition of delirium and an etiology-related definition of acute encephalopathies. To include both the clinical phenotype and the underlying brain disorder, the overarching term 'delirium disorder' has been introduced [3].

Risk of long-term cognitive impairment

Delirium disorder is a well-established independent risk factor for long-term cognitive dysfunction, incident dementia and worsening of existing dementia [4]. In a study with high power, including 650,590 non-demented elderly, who were followed for more than 5 years, patients with delirium had 39% higher risk of death and a three times higher risk of incident dementia than those without delirium [5]. It should, however, be noted that an independent association does not necessarily represent causation.

An increasing number of studies underpins detrimental effects of acute encephalopathy that manifests as delirium. Several important and extensively studied domains

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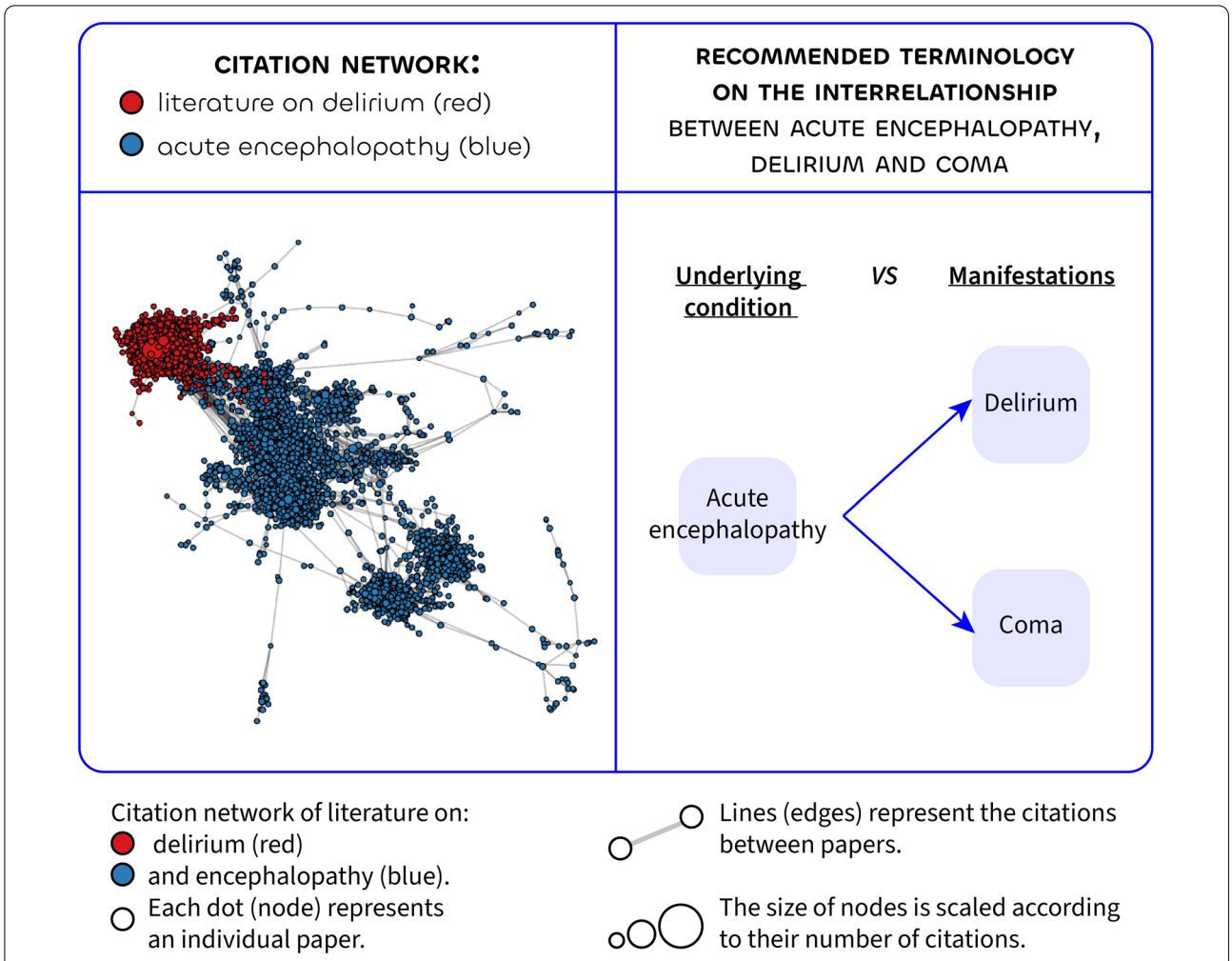
CITATION NETWORK:
literature on delirium (red)
acute encephalopathy (blue)
RECOMMENDED TERMINOLOGY ON THE INTERRELATIONSHIP BETWEEN ACUTE ENCEPHALOPATHY, DELIRIUM AND COMA
Underlying condition
VS
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Delirium
Acute encephalopathy
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Citation network of literature on:
delirium (red)
and encephalopathy (blue).
Each dot (node) represents an individual paper.
Lines (edges) represent the citations between papers.
The size of nodes is scaled according to their number of citations.

Fig. 1 Citation network of literature on delirium (red) and encephalopathy (blue). Each dot (node) represents an individual paper. Lines (edges) represent the citations between papers. The size of nodes is scaled according to their number of citations. Node positioning is based on an iterative force directed layout algorithm which causes highly connected sets of nodes to cluster together. This figure shows that the literature on delirium and encephalopathy is highly segregated

have shown promising association with delirium—neuroinflammation, neuronal injury and neurotransmitter imbalance. To get an insight into more comprehensive understanding of the neurobiological mechanisms in this complex setting it is necessary to move beyond association and find true causal pathways [6]. Experimental research using animal models important, yet studies in humans are of critical importance [7, 8]. An approach using modern causal interference techniques, such as target trial emulation can be used to better analyze RCTs and establish this relationship.

Sedation-related and other phenotypes of delirium

Having said that acute encephalopathy is the pathobiological process in the brain, it is important to distinguish different phenotypes of ICU delirium as distinct clinical manifestations (i.e. hypoxic, septic, metabolic, sedative, unclassified) with a notion that sedation-related delirium differs from other types as it has different outcomes [9]. Factors such as sedative choice, depth of sedation, and the specific delirium assessment tool used are crucial in both clinical practice and research on sedation-related delirium, but other overlapping reasons should also be acknowledged (i.e., sepsis, electrolyte derangements, hypoxemia, central nervous system injury, alcohol intoxication or withdrawal, hyper or hypo-glycemia and extreme vitamin deficiencies).

Patel and colleagues evaluated patients in the context of delirium before and after sedatives were stopped. Despite methodological limitations (i.e., uncontrolled

design, limited adjustment for confounders, predominant use of propofol, and focus on short-term outcomes), the key contribution was the observation that rapidly reversible, sedation-related delirium may be associated with more favorable outcomes compared to other delirium subtypes as the patients with sedative-induced delirium had identical survival outcomes to those who had no ICU delirium at all [10].

Obviously, the treatment of these different reasons is founded in an understanding of the cause of delirium disorder.

Future studies

Future studies should explore how emerging terminology—such as that proposed by Slooter et al.—can improve diagnostic accuracy, interdisciplinary communication, and the evaluation of patient outcomes such as long-term cognitive function, functional recovery, and quality of life [2].

Another pathway for future pragmatic studies lies within the need to train different medical specialties in understanding how new consensus-based, pragmatic nomenclature can challenge billing or reimbursement if different codes are used. Currently, it is financially more lucrative in the DRG system in the US to code an episode as 'encephalopathy' than as 'delirium', but efforts were made to achieve parity between delirium and acute encephalopathy in the MS-DRG system [11].

Moreover, more studies are needed to examine how clinical assessment of delirium aligns with EEG-based classification of acute encephalopathy, to determine whether EEG findings could offer added value to expert clinical evaluations. Research should focus on ways to distinguish between hypoactive delirium and non-delirious states or identify subclinical cases that may be missed during bedside assessment. Combining EEG markers of acute encephalopathy with clinical criteria for delirium may represent a promising reference framework for future research, particularly in the validation of delirium detection methods that incorporate EEG data and include AI-aided diagnostic tools [12–14].

Future research should also focus on long-term cognitive impairment and sedation-related delirium, as these are critical areas where knowledge gaps remain and where improved understanding could directly impact patient outcomes [6].

Conclusion

Limitations of current terminology and the ongoing use of "encephalopathy" versus "delirium" in clinical practice and research dichotomizes the approach instead of unifying it. Expert panel regarded acute encephalopathy to be the pathobiological process in the brain, and delirium as a possible phenotypic manifestation of this process. Delirium disorder, including both clinical phenotype and underlying brain disorder, is a common problem in the ICU and perioperative care with substantial morbidity and mortality [4]. Although no randomized trials have directly tested the impact of ICU delirium screening or terminology improvement on outcomes, strong evidence from cohort studies—particularly those evaluating the ABCDEF bundle—supports routine delirium monitoring as part of comprehensive care. In line with the 2018 PADIS and 2024 ESAIC guidelines [15], regular screening should be considered standard practice to support early recognition and intervention.

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Declarations

Conflicts of interest

KK is a Section Editor for Intensive Care Medicine. She has not taken part in the review or selection process of this article.

Ethics statement

An approval by an ethics committee was not applicable.

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